

Application No. 10/060,759
Office Action dated January 17, 2006
Amendment mailed July 17, 2006

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REMARKS

Applicant has amended the title to remove the recitation to compositions as requested by the Examiner. This amendment is clerical in nature; therefore, it does not introduce new matter, and its entry is respectfully requested.

Applicant has amended claim 15 by deleting the phrase "referred to as XX5." The amendment is clerical and does not introduce new matter. The entry of the amendment is respectfully requested.

The title was objected because it referred to compositions as well as methods. Applicants have amended the title to remove the recitation to compositions. Accordingly, the objection to the title has been obviated.

Claim 15 was objected to because of the use of the phrase "referred to as XX5." Applicants use the generic compound name in the claim, and thus have deleted the phrase. Accordingly, the objection has been obviated. Therefore, Applicant submits that claim 15 is in condition for allowance.

Claims 1-7 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vassallo et al., Mayo Clinic Proceedings ("Vassallo").

Applicant disagrees, and submits that this rejection should be withdrawn for the following reasons.

Claims 1-7 are directed to using **specific PDE4 inhibitors** to treat chronic lymphocytic leukemia (CLL). There is a difference between a PDE inhibitor and a **specific PDE4 inhibitor**. As explained in the previous amendment, there are a range of PDE inhibitors such as PDE I, PDE II and PDE VII. This is neither taught nor suggested by Vassallo.

Theophylline is not a specific PDE4 inhibitor. It is not even a specific PDE inhibitor. Indeed, Vassallo specifically teaches that the **mode of action** of theophylline is **poorly defined** (p. 346, 2nd col.). Theophylline is described to **have a number of different actions** at cellular level,

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including generally inhibiting phosphodiesterases (PDEs) (p. 346, abstract, and under subtitle "Phosphodiesterase Enzyme Inhibition" bridging pp. 346 and 347). Moreover, Vassallo also states that the **"mechanism by which theophylline induces apoptosis is unclear"** (p. 351, 1st col., second to last sentence). Vassallo further describes various uses for theophylline for potentially treating a number of different diseases, including induction of apoptosis of CLL cells (p. 351, left col. 3rd full par.). Accordingly, without more, what Vassallo teaches and or suggests is only the potential to use theophylline for the treatment of CLL. The specific advantage of using a specific PDE4 inhibitor is neither disclosed, nor suggested.

The Examiner contended in the July 25, 2005 Office Action (p. 3) that **in the absence of evidence to the contrary**, it would have been obvious to treat a patient with CLL using theophylline, a non-specific PDE inhibitor. While Applicant disagrees with the Examiner's statement – the claims do not cover using theophylline because as explained above, it is not a specific PDE4 inhibitor. Further, the Examiner **ignores the specific evidence shown within the four corners of the specification**. Namely, the Applicant specifically shows that **only a specific PDE4 inhibitor** has a beneficial effect. As discussed already in the Amendment dated October 25, 2005, for example, in Example 3, Applicant clearly showed that only PDE4, not PDE1, induced apoptosis in CLL cells (see, e.g., page 17 of the specification).

Also, as already pointed out by the Applicant in the Amendment dated October 25, 2005, at page 347, third full paragraph, lines 26-27, Vassallo et al. contemplates that there may also be other PDEs that have not yet been discovered that are sensitive to inhibition from theophylline. Moreover, at page 348, Vassallo pointed out that **there are differences between specific PDE4 inhibitors and the nonselective PDE inhibitor, theophylline**. Specifically, a distinction is made between theophylline and the prototypical PDE type IV inhibitor, rolipram, at page 348, where Vassallo shows that **a specific PDE4 inhibitor did not have the same effect as theophylline** (Vassallo at page 348, first column). Accordingly, it would **not** be obvious to use PDE4 inhibitors instead of theophylline.

Applicant respectfully submits that Vassallo et al. does not render the present invention obvious. Vassallo does not suggest the use of a PDE4 inhibitor any more than a PDE1 inhibitor,

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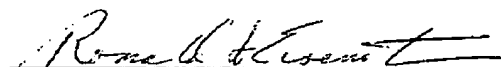
or a PDE VII inhibitor, etc. Nor does Vassallo suggest that any PDE inhibitor would be effective against CLL. Accordingly, this rejection should be withdrawn.

In view of the foregoing, Applicant respectfully submits that all claims are in condition for allowance, or that at minimum, the issues in Appeal will be reduced. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our Deposit Account No. 19-2380.

Respectfully submitted,

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